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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER

HM21/0928

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ART UNIT	PAPER NUMBER
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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-13 is/are pending in the applicati
Of the above, claim(s) _____ is/are withdrawn from considerati
☒ Claim(s) 1-13 is/are allowed.
☐ Claim(s) _____ is/are rejected.
☐ Claim(s) _____ is/are objected to.
_____ are subject to restriction or election requirem

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES

DETAILED ACTION

1. Claims 1-13 are pending and under examination.

Claim Rejections - 35 USC § 112

2. Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of the specifically claimed monoclonal antibodies produced by the hybridoma HB_3cB_3 and $RcB_3M_1D_4$ deposited with the American Type Tissue Collection (ATCC™). Applicant's referral to the deposit of the hybridoma cell lines producing these antibodies in the text of the specification is an insufficient assurance that all required deposits have been made and all the conditions of 37 CFR §1.801-1.809 have been met.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that (a) the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and (b) that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. In addition, amendment

of the specification to recite the date of deposit and the complete name and full street address of the depository is required. It is noted that the address of the ATCC has changed to American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridoma cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

3. Claims 6 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 6, the claim is confusing because, apolipoprotein by definition has no lipid associated with it, lipid becomes associated with the apolipoprotein as it is formed inside the cell and secreted as a lipoprotein. Thus, the only lipoproteins which contain apolipoproteins have lipid associated with them and the recitation of the amount of apolipoprotein-associated lipid is highly confusing.

As to claim 9, this claim is confusing as it depends from claim 6 and ultimately from claim 1, uses multiple antibodies and the claim structure does not provide for clear antecedent basis for each of the antibodies and thus the term "antibody" in the claim fails to provide for clear antecedent basis. The examiner suggests the use of a "first antibody" and "second antibody" to provide for clear antecedent basis.

Claim Rejections - 35 USC § 102 or 103

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. It is noted that claim 1, appears to detect the lipoprotein/apolipoprotein in the alternate with lipid associated with lipoprotien/apolipoprotein. Inasmuch as, this is the only reasonable interpretation of this claim it has been examined as depending from claim 1, for art purposes only.

7. Claim 1, 2, 10, and 11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Forster et al (Biochem. Soc. Trans. 18(6):1180, December 1990).

Forster et al teach the development of a simple dipstick measurement of apolipoproteins. Forster et al teach a sandwich assay for Apo AI or Apo B, wherein one of the antibodies is bound to the dipstick. The dipstick is immersed into the sample. After a certain amount of time the stick is removed and immersed in a developing reagent to detect Apo AI or Apo B. The presence of Apo AI or Apo B is detected using an enzyme-labeled second antibody or added to the sample a small amount of the corresponding enzyme-labeled apolipoprotein which acts as a tracer. Forster et al teach that Apo AI and Apo B are the major protein components of high-density lipoproteins (HDL) and low-density lipoproteins (LDL) respectively.

8. Claims 1, 2, 3, 10, 11, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scripps Clinic (EP 0 257 778, published 2/3/88) in view of Forster et al (Biochem. Soc. Trans. 18(6):1180, December 1990).

Scripps Clinic (EP 0 257 778, published 2/3/88) teaches an indirect solid phase immunoassay for Apo B100 using two monoclonal antibodies wherein one monoclonal antibody is immobilized on a solid phase and the other labeled monoclonal antibody to a second epitope is

added to the sample to form an immunoreaction mixture before contacting with the solid phase (page 13, see lines 38-42). Scripps differ by not teaching a dipstick immunoassay format.

Forster et al is set forth *supra*.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase assay of Scripps Clinic by employing as the solid phase the dipstick of Forster et al because Forster et al teach that apolipoproteins can be measured by a simple dipstick immunoassay and the substitution of one solid phase for another is routine in the art. It would have also been *prima facie* obvious to one of ordinary skill in the art to use antigen binding fragments or recombinant antibodies in the method as combined above because these would function equivalently in the assay as combined and such substitutions are routine in the art.

9. Claims 1, 2, 3, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luca (EP 0 407 035, published 2/3/88) in view of Forster et al (Biochem. Soc. Trans. 18(6):1180, December 1990).

Luca teaches a method for the determination of lipid and/or apoprotein moiety of intact lipoproteins. Luca teaches capturing lipoproteins in a biological sample with an antibody (i.e. polyclonal, monoclonal claims 1-2; page 19) immobilized on a solid support which binds and epitope on an apolipoprotein and staining at least one fraction of the lipid contained in the lipid moiety of the captured lipoprotien by means of a lipid probe which becomes incorporated into the lipid moiety of the captured lipoprotein, detecting the measured signal form the incorporated or attached lipid probe and relating the signal identity to the amount of the fractions of the lipid moiety. Luca teach that the determination of lipoproteins and lipids are important in the

examination of coronary heart disease. Luca differ by not teaching a dipstick immunoassay format.

Forster et al is set forth *supra*.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase assay of Luca by employing as the solid phase the dipstick of Forster et al because Forster et al teach that apolipoproteins found in lipoproteins in body fluids can be captured by a simple dipstick immunoassay and the substitution of one solid phase for another is routine in the art. It would have also been *prima facie* obvious to one of ordinary skill in the art to use antigen binding fragments or recombinant antibodies in the method as combined above because these would function equivalently in the assay as combined and such substitutions are routine in the art.

10. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luca (EP 0 407 035, published 2/3/88) in view of Forster et al (Biochem. Soc. Trans. 18(6):1180, December 1990) as applied to claims 1, 2, 3, and 6 above and further in view of Mills et al (Laboratory Techniques in biochemistry and molecular biology, Volume 14, A Guidebook to Lipoprotein Technique; 1984, pages 472-478).

Luca (EP 0 407 035, published 2/3/88) in view of Forster et al (Biochem. Soc. Trans. 18(6):1180, December 1990) as combined differ by not teaching the lipid stains Oil Red O and Sudan Black B.

Mills et al teach conventional and routine methods of staining lipids using routine and conventional stains such as Oil Red O and Sudan Black B (page 473-475). Mills et al also teach that Sudan Black can be used to pre-stain lipoproteins in plasma.

As to claim 7, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute Oil Red O or Sudan Black B for the lipid stain in the method as combined because Mills et al teach that lipids are conventionally detected using the Oil Red O and Sudan Black B. As to claim 8, it would have been *prima facie* obvious to one of ordinary skill in the at the time the invention was made to pre-stain the sample lipoproteins in the method as opposed to subsequent staining of the lipoproteins using the prestaining method with Sudan Black B as taught by Mills et al because Mills et al teach that the lipoproteins in a plasma sample can be detected even if they are prestained.

11. Claims 1, 2, 3, 10, 11, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scripps Clinic (EP 0 257 778, published 2/3/88) in view of Rounds (U.S. Patent 4,786,589).

Scripps Clinic (EP 0 257 778, published 2/3/88) teaches an indirect solid phase immunoassay for Apo B100 using two monoclonal antibodies wherein one monoclonal antibody is immobilized on a solid phase and the other labeled monoclonal antibody to a second epitope is added to the sample to form an immunoreaction mixture before contacting with the solid phase (page 13, see lines 38-42). Scripps Clinic differ by not teaching a dipstick immunoassay format.

Rounds et al teach a dipstick immunodot procedure for detecting the presence of a target protein in a test fluid comprising mixing the test fluid with a forzman-labeled-antibody which specifically binds the antigen of interest to form an immunoreaction mixture, immersing into the mixture a dipstick on which is mounted a membrane having immobilized thereon antibodies which specifically bind the antigen but are not labeled, removing the dipstick from the mixture after a select period of time and visually inspecting the dipstick for the presence of antigen (columns 9-10). Rounds et al teach that the forzman dye is a protein dye and other protein

specific dyes may be substituted for the forzman (see column 5, lines 39-45). Rounds teaches that the dipstick immunodot procedure is appropriate for the detection of a wide variety of antigens. Rounds teaches that the one step immunoassay decreases the risk for error compared to multi-step solid phase assays of the art, especially when performed by an unskilled person (column 1, lines 1-37).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase assay of Scripps Clinic by employing as the solid phase format the dipsticks format of Rounds et al because Rounds teaches that the dipstick immunodot procedure is appropriate for the detection of a wide variety of antigens and that the one step immunoassay decreases the risk for error compared to multi-step solid phase assays of the art, especially when performed by an unskilled person apolipoproteins can be measured by a simple dipstick immunoassay and the substitution of one solid phase for another is routine in the art. It would have also been *prima facie* obvious to one of ordinary skill in the art to use antigen binding fragments or recombinant antibodies in the method as combined above because these would function equivalently in the assay as combined and such substitutions are routine in the art.

12. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Luca (EP 0 407 035, published 2/3/88) in view of and Forster et al (Biochem. Soc. Trans. 18(6):1180, December 1990).

Luca teaches a method for the determination of lipid and/or apoprotein moiety of intact lipoproteins. Luca teach a variant method for detecting and for measuring both a lipid moiety and an apolipoprotein moiety of an intact lipoprotein contained in a sample of body fluid or tissue. Luca teaches capturing lipoproteins in a biological sample with an antibody (i.e. polyclonal,

monoclonal claim 17-24, page 20) immobilized on a solid support which binds and epitope on an apolipoprotein and staining at least one fraction of the lipid contained in the lipid moiety of the captured lipoprotien by means of a lipid probe which becomes incorporated into the lipid moiety of the captured lipoprotein, detecting the measured signal form the incorporated or attached lipid probe and relating the signal identity to the amount of the fractions of the lipid moiety, detecting and measuring at least one apolipoprotein moiety by means of a labeled antibodies and relating the detection and measurement of the expressed epitope to the amount of apolipoprotein in the sample. Luca teach that the determination of lipoproteins and lipids are important in the examination of coronary heart disease. Luca differ by not teaching a dipstick immunoassay format or prestaining the detection antibody coupled to a protein stain.

Rounds et al teach a dipstick immunodot procedure for detecting the presence of a target protein in a test fluid comprising mixing the test fluid with a forzman-labeled-antibody which specifically binds the antigen of interest to form an immunoreaction mixture, immersing into the mixture a dipstick on which is mounted a membrane having immobilized thereon antibodies which specifically bind the antigen but are not labeled, removing the dipstick from the mixture after a select period of time and visually inspecting the dipstick for the presence of antigen (columns 9-10). Rounds et al teach that the forzman dye is a protein dye and other protein specific dyes may be substituted for the forzman (see column 5, lines 39-45). Rounds teaches that the dipstick immunodot procedure is appropriate for the detection of a wide variety of antigens. Rounds teaches that the one step immunoassay decreases the risk for error compared to multi-step solid phase assays of the art, especially when performed by an unskilled person (column 1, lines 1-37).

Forster et al teach the development of a simple dipstick measurement of apolipoproteins. Forster et al teach a sandwich assay for Apo AI or Apo B, wherein one of the antibodies is bound to the dipstick. The dipstick is immersed into the sample. After a certain amount of time the stick is removed and immersed in a developing reagent to detect Apo AI or Apo B. The presence of Apo AI or Apo B is detected using an enzyme-labeled second antibody or added to the sample a small amount of the corresponding enzyme-labeled apolipoprotein which acts as a tracer. Forster et al teach that Apo AI and Apo B are the major protein components of high-density lipoproteins (HDL) and low-density lipoproteins (LDL) respectively.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the combined assay of Luca to by employing as the solid phase format the dipstick formats of Rounds et al and Forster et al because Rounds teaches that the dipstick immunodot procedure is appropriate for the detection of a wide variety of antigens and that the one step immunoassay decreases the risk for error compared to multi-step solid phase assays of the art, especially when performed by an unskilled person apolipoproteins can be measured by a simple dipstick immunoassay and the substitution of one solid phase for another is routine in the art and Forster et al teach the development of a simple dipstick measurement of apolipoproteins to measure the major protein components of high-density lipoproteins (HDL) and low-density lipoproteins (LDL) respectively and Luca teaches that the measurement of both lipids and lipoproteins/apolipoproteins are useful because they are linked to coronary artery disease.

Status of Claims

13. No claims are allowed.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Patricia A. Duffy, Ph.D.
September 26, 1998

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600